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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,850	08/04/2003	Linda Hanley-Bowdoin	5051-458IP	5547

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EXAMINER	
ZHENG, LI	
ART UNIT	PAPER NUMBER
1638	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/633,850	HANLEY-BOWDOIN ET AL.	
	Examiner	Art Unit	
	Li Zheng	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-28* is/are pending in the application.

4a) Of the above claim(s) *19 and 22-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 August 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12102003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group V, claim 20, and SEQ ID NO: 109, cancellations to claims1-18, as well as addition of claims 21-28 in the reply filed on 9/11/2006 are acknowledged.

The newly added claim 21 belongs to Group V, whereas claims 22-26 belong to a separate invention that is drawn to a method of using the nucleotide sequence/vector of Group V. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be

maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The traverse is on the ground(s) that Groups IV and V are in the same class and subclass (response, page 5, the 4th paragraph) and there is no serious search burden to search all the sequences in claim 20 (response, page 5, the 4th paragraph). There is a typographic error in the classification of Group V in previous office action, and the correct classification for Group V is class 536, subclass 23.2. The polypeptide of invention IV and polynucleotide of invention V are patentably distinct inventions for the reasons clearly stated in the previous office action (the paragraph bridging pages 2-3).

The examiner also maintains that the search and examining of all sequences in claim 20 is undue. Applicants are reminded that nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute **independent and distinct** inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such

nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq.

Non-elected subject matter must be removed from the claims.

The requirement is still deemed proper and is therefore made FINAL.

Specification

2. The disclosure is objected to because of the following informalities:

Page 1, line 4 recites a U.S. Patent application number. The status of this application should be indicated.

Appropriate correction is required.

3. The specification is objected to under 37 CFR 1.821(d) as failing to refer to a sequence by use of its sequence identifier preceded by "SEQ ID NO:". The polypeptide sequences in Figures 3 and 11 (consensus sequence) should be identified as SEQ ID NOs. Alternatively, the brief descriptions of those figures on pages 7 and 11 can be amended to recite the identifiers.

4. The drawings are objected to because the labels for AL1 mutants in Figure 4 (A) are inconsistent with the information disclosed elsewhere in the specification. For example, "N-DR171" in Figure 4 (A) is labeled as "N-DR172" in

Fig. 3, 5, 6 and Table 3. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Priority

45. SEQ ID NO: 109 is not supported by the parent application, therefore, the priority date for the instant invention is 8/4/2003.

Claim Objections

6. Claim 20 is objected to for depending from a non-elected claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification, particularly in example 7, teaches that the RBR1 binding domain of AL1 protein from TGMV was mapped to between amino acid 101-180 by using yeast two hybrid system and mutations in residue KEE146 have been shown to impair binding (page 37 lines 24-30 and page 38, lines 19-20). Further analysis of additional alanine substitution mutant indicates that E145, E146 and EE146 mutation did not alter AL1/RBR1 binding significantly, whereas K144 mutation reduced RBR1 interaction to 42% (page 39, lines 1-7). Since KEE constitute the first three residues of an 11 amino acid motif, Helix 4, more mutations were generated within the region and analyzed. Although the A147

and II151 mutants displayed significantly lower RBR1 binding activities than wild type AL1, these mutations also showed reduced AL1 oligomerization activity, indicating that their effects are not specific for RBR1 binding (page 39, lines 20-23). In contrast, the L148 mutation reduced the AL1/RBR1 interaction to 25% of wild type level without a concomitant loss in AL1 oligomerization activity, thereby establishing the specificity of the mutation for RBR1 binding (page 39, lines 23-26). Plant infection experiments were carried out by co-bombarding either wild type or mutant A component DNA with a TGMV B replicon onto N. benthamiana plant. The K144, E145, E146 and EE146 mutants develop wild type symptoms with a similar timing. Mutants A147 and II151 produced no detectable symptoms even after 5 week post-inoculation. In contrast, the L148 mutant produced milder symptom that appeared 14-21 days post infection. L148-infected plants displayed no stunted growth or leaf curling, and only developed chlorosis along the veins, which is similar to those of KEE146-infected plants (page 40, 2nd paragraph). DNA blot analysis showed that the difference in TGMV DNA level between L148- and wild-type TGMV-infected plants are stable over time, suggesting that the attenuated symptoms caused by the L148 mutation are likely due to reduced RBR1 binding (the paragraph bridging pages 40-41). Various mutations were further generated at the position L148 and analyzed in yeast two hybrid system. It was concluded that the binding activities of the mutant declined with the probability of the substituted amino acid to occur in an alpha-helix and the reduced RBR1 binding activities are not due to a general destabilization of AL1 (page 41, lines 17-23). To determine if RBR1 binding is a general property of

begomovirus replication proteins, Gal4 AD fusions corresponding to full-length TYLCV and CbLCV AL1 were generated and tested for interaction with DBD-RBR1 fusion. The RBR1 binding activity of TYLCV C1 was similar to that for TGMV AL1, in contrast, CbLCV full-length AL1 fusion are toxic to the host cell. Therefore, amino acids 1-178 of CbLCV were used to generate fusion protein and a reduced but significant level of RBR1 binding was detected (the paragraph bridging pages 41-42). The substitution of an alanine at position L145 in CbLCV AL1 was examined for the ability to impair RBR1 binding analogous to the TGMV L148 mutant. The CbLCV L145A and TGMV L148 mutations reduced RBR binding to 23% and 25% of their respective wild type controls.

However, the specification does not teach expression of oligomerization domain of SEQ ID NO: 109 from CbLCV or oligomerization domain of L148 from TGMV could reduce wild type replication as those oligomerization-domain-fused GST mutants Ala6-9 and Ala 13-14 do in Example 5 (page 35, lines 5-16). The specification shows that mutation of L145 in CbLCV AL1 impair RBR1 binding analogous to the TGMV L148 mutant and L148-infected plants displayed a phenotype similar to those of KEE146-infected plants. However, Figure 3 and tables 1 & 2 show that the ability of Ala5 oligomerization domain (KEE146 mutant) alone to interfere with wild type replication is not confirmed (page 43). Furthermore, as discussed above, various mutations even within the motif, helix 4, produce dramatically different phenotypes in plant infection experiment, therefore, the ability of specific mutant to interfere with wild type replication is unpredictable. Without further guidance , undue experimentation would be

required for a person skilled in the art to determine the ability of the oligomerization domain of SEQ ID NO: 109 to interfere with wild type CbLCV replication. See *Genentech Inc. v. Novo Nordisk,* A/S (CA FC) 42 USPQ2d 1001 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Desbiez et al. (1995, PNAS 92:5640-5644).

Desbiez et al. teach PUC118 based vector containing mutant Rep gene (also known as C1 or AL1) from TYLCV (page 5640, 2nd paragraph of the left column and page 5641, the last paragraph of the left column). The instant claims are drawn to nucleotide sequences/vector comprising an isolated nucleotide sequence encoding a mutant AL1 comprising a amino acid sequence of SEQ ID NO: 109 (emphasis added), which encompasses any AL1 mutant protein comprising at least two residues of SEQ ID NO: 109. The reference therefore teaches all the limitation set forth by instant claims.

Conclusion

Claims 20 and 21 are rejected.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ELIZABETH MCELWAIN
PRIMARY EXAMINER